More Clues to the Cause of Parkinson's Disease

Indications that more patients are developing Parkinson's disease at a young age, and that families cluster in their time, but not age, of onset, bolster the environmental hypothesis for the cause of the disease

"THE reason we did the study was that several of us were getting the impression that we were seeing more and more young patients with Parkinson's disease," explains Donald Calne of the University of British Columbia. "It seems to me that, even with these limited data, the numbers in the young age group—below 50 years—might have increased by as much as 50% over the past 30 years or so."

The implication of these findings—if confirmed—is that "It is difficult to avoid the conclusion that there is an environmental risk factor [in the disease process] which is becoming more common," suggest Calne and his colleagues.

The notion that some kind of environmental agent might be involved in the cause of Parkinson's disease—and certain other neurological conditions—has been gaining popularity in recent times, with Calne as one of its principal proponents. One reason is that a number of recent twin studies appear to preclude genetic factors as playing a dominant role in the etiology of Parkinson's, even though they might exert some influence on an individual's susceptibility to the disease. Another is the discovery that a contaminant—known as MPTP—of a synthetic heroin can cause parkinsonian-like symptoms in humans and animals, which alerted researchers to the possibility that similar agents in the environment might play a role in the natural disease.

Clearly, a shift in the age pattern of the disease would be consistent with an environmental rather than a genetic hypothesis.

This putative shift has been noticed by others. "Yes, I've heard people say that they are seeing more young-onset Parkinson's patients," says William Langston of the Institute of Medical Research, San Jose. "And I think I see the same thing in our clinic. But you have to be very careful because, with the recent upsurge in interest in Parkinson's, perhaps clinicians are looking harder than they did previously."

Ira Shoulson, of the University of Rochester Medical Center, agrees. "I'm sure there is a general perception among clinicians that they are now seeing more young-onset Parkinson's patients," he says. That perception is, however, based on unsystematic, anecdotal evidence.

The data that Calne and his colleagues recently published are, however, merely suggestive of a trend and by no means confirm one. This shortfall results principally from the nature of the data themselves, which initially come from information on the age of onset of the disease among hospital patients in Vancouver and Helsinki between 1982 and 1985. These two populations, numbering 355 and 196 respectively, show 8% of patients developing the disease below the age of 40. These age of onset profiles can be converted to prevalence of the disease in different age groups, and then compared with prevalence data from earlier studies.

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The problems arise from the comparisons, because the constitution of the different populations usually differs enormously, making clear-cut answers almost impossible. Data from a study of prevalence in Rochester, New York, between 1935 and 1966 do, however, offer a reasonable comparison, and Calne and his colleagues conclude that "the possibility that a real difference exists has to be considered." It is upon these data that Calne makes his estimate of a 50% increase in the young onset group.

Calne stresses that these findings do not portend an epidemic in Parkinson's disease, merely oscillations in the epidemiology. "The important lesson," he suggests, "is that these shifts reflect shifts in environmental factors over time and tell us about the nature of the disease." Although the pieces of the jigsaw are coming together in various forms, "the central picture is not yet clear, but we are beginning to see the outside framework," he says.

That picture may begin to clear a little with a project that is likely to be initiated in October by the newly formed Parkinson Study Group. The group is due to meet in San Francisco on the eve of the annual meeting of the American Neurologic Association, on 18 October. "We hope to encourage clinicians to pool their data on age of onset," says Shoulson, one of the founders of the group, "and then we will be able to get a better idea of whether the perceived shift to younger ages is real."

Meanwhile, Calne and his colleagues have other data that point to environmental factors playing a role in the the disease, at least in some cases. Specifically, they looked at families in which more than one member developed Parkinson's disease. If the disease were the result strictly of genetic influence, then the different family members would be expected to develop the condition at roughly the same age, they argue. But if exposure to environmental toxins—perhaps transiently appearing—were important then onset of the disease might occur at roughly the same time within the family, but at very different ages for parents and offspring.

"We consider that at least half of the familial clustering which we have observed conforms to the [environmental factor] pattern," conclude Calne and his colleagues. For instance, in a current paper in which they describe six such families, there is in one case a mother, father, and offspring who developed Parkinson's disease. Although their ages at onset, respectively 68, 58, and 37 years, were very different, the years in which the disease occurred were very close—1964, 1961, and 1963. "The clustering of time of onset, not age, is remarkable," says Calne.

"We are not arguing against the existence of any genetically determined cases of parkinsonism," say Calne and his colleagues. "We are merely reporting evidence that some familial cases are likely to be of environmental origin." The key question—what in the environment might be the culprit(s)—remains to be solved. ■

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ADDITIONAL READING

H. Teravainen *et al.*, "The age of onset of Parkinson's disease," *Can. J. Neurol. Sci.* **13**, 317 (1986).

S. Calne *et al.*, "Familial Parkinson's disease," *ibid.* **14**, 303 (1987).